EXHIBIT H

In the matter of an opposition by Chiron Corporation to European Patent EP 139417 (84305909.8) of Genentech Inc.

STATUTORY DECLARATION

I, DAVID S. SECHER, do solemly and sincerely declare as follows:

1. I am a citizen and resident of the United Kingdom.

2. I received my undergraduate training in Biochemistry from the University of Cambridge. I completed my Ph.D. in 1974, in the Medical Research Council Laboratory of Molecular Biology at the University of Cambridge under the direction of C. Milstein, an eminent immunologist and Nobel Laureate.

3. I am currently engaged as a Biotechnology Consultant and prior to this I was the director of a research effort of Celltech Ltd. In that position, I had overall responsibility for the development of novel, monoclonal antibody-based therapies.

4. I was a member of the scientific staff at the Medical Research Council Laboratory of Molecular Biology, Cambridge for thirteen years.

5. I have been on the editorial boards of Biological Reviews and Revista Biologica and am currently an editor for the journal Drug Design and Delivery.

6. I have published extensively in the broad area of immunology with specific focus on somatic mutations in antibody genes, the characterization of monoclonal antibodies, and human

interferon. This focus naturally extends to a research interest in the prevention of viral pathogenesis and in support of this interest, I have published on research relating to papilloma, rhinovirus and Sendai virus. I have attached as an integrated appendix a list of these publications.

7. I am generally familiar with the subject matter of the above-mentioned Genentech patent, European Patent 139417 B, and with the publications of Phillip Berman and Laurence Lasky relating to their invention of a Herpes Simplex virus vaccine.

8. I am also familiar with the work reported in the references cited by the opponents.

9. As a working premise, I use the term "vaccine" in accord with the standard scientific definition. A "vaccine" protects animals against pathogenic infection by raising immunity in the animal against the pathogen. Thus, "vaccine" has the provision of protection of the animal against a pathogen by affording immunity via some component of the immune system. An entity that raises "neutralizing antibodies" is not a part of the definition of "vaccine" because raising neutralizing antibodies may be required but is certainly not itself sufficient to provide protective immunity.

10. I was asked to comment specifically on the work of Cohen et al., reported at the Eighth International Herpes Virus Workshop, Oxford, England (31 July 1983); (Reference L). For the reference to be able to support a vaccine, a definition would have to be accepted that included any substance that stimulates the production of neutralizing antibodies whether or not those

antibodies have any influence on the course of disease. The demonstration of the neutralizing antibodies was obtained from an in vitro system. There is no evidence in the reference to any benefit to animals (i.e., in vivo) in terms of protection against infection with virus or prevention of spread of the virus. Therefore, I conclude that Reference L does not enable a "vaccine" as such. (See Paragraph 9).

11. After reviewing the publications of Phillip Berman and Laurence Lasky relating to their invention of a Herpes Simplex virus vaccine, I concluded that their data was convincing. The scientific strength of this research resides in the use of a truncated version of a single glycoprotein from the rather complex model Herpes Simplex virus to confer protective immunity in the animal against the pathogen. The Berman and Lasky work provided a recombinantly produced truncated polypeptide that survived in vivo to give such protective immunity. Therefore, the Berman and Lasky results conform with the preparation of a successful vaccine that provides protective immunity in vivo against pathogenic challenge. The publication of these results provided researchers with encouragement that similar efforts would lead to success with analogous viral pathogens.

12. Further, as viruses are generally complex mosaics of various components including glycoproteins, that are arranged conformationally in a specific way, it could be supposed that this conformation is likewise required for immunoprotective antibody recognition.

13. At the time this invention was first disclosed (August

1983), one of ordinary skill in the art could not have reasonably predicted the successful preparation of an in vivo vaccine based solely on the essential presence of but one glycoprotein from the herpes simplex virus mosaic, produced as a recombinantly derived, truncated derivative that was not associated with its membrane domain.

AND I MAKE this solemn declaration, conscientiously believing the same to be true, and by virtue of the Statutory Declarations Act 1835

David S. Secher

Merlin Place Cambridge 29/1/91
place date

Before me: G.W.A. Chadwick

SOLICITOR
G.W.A. CHADWICK

MAIN PUBLICATIONS

1 Van Heyningen S & Secher DS "A new alkaline protease from *Acremonium kiliense*" Biochemical J 125 1159-1160 (1971)

2 Bridgen J & Secher DS "Molecular heterogeneity of alkaline phosphatase" FEBS Letters 25 55-57 (1973)

3 Cotton RGH Secher DS & Milstein C "Somatic mutation and the origin of antibody diversity. Clonal variability of the immunoglobulin produced by MOPC 21 cells in culture" Eur J Immunol 3 135-140 (1973)

4 Cowan NJ Secher DS Cotton RGH & Milstein C "The secretion of a sialic acid-free immunoglobulin" FEBS Letters 30 343-346 (1973)

5 Secher DS Cotton RGH Cowan NJ & Milstein C "Spontaneous mutation in immunoglobulin genes" in "The Immune System" (eds Sercarz EE & Fox CF) pp353–355 Academic Press New York (1974)

6 Bennich H Milstein & Secher DS "Human immunoglobulin E. The primary structure of the C-terminal domain of the epsilon chain" FEBS Letters 33 49-53 (1973)

7 Secher DS Cotton RGH & Milstein C "Spontaneous mutation in tissue culture - chemical nature of variant Ig from mutant clones of MOPC 21" FEBS Letters 37 311-316 (1973)

8 Milstein C Cotton RGH & Secher DS "Variability of immunoglobulins" Annales Immunol (Institute Pasteur) 125C 287-308 (1974)

9 Milstein C Secher DS Cowan NJ Harrison TM Cotton RGH & Brownlee GG "Immunoglobulin mRNA, immunoglobulin mutants and the integration of two genes into one polypeptide" in "Cellular Selection and Regulation in the Immune Response" (ed. Edelman GM) pp245-264 Raven Press New York (1974)

10 Milstein C Adetugbo K Cowan NJ & Secher DS "Clonal variants of myeloma cells" in "Progress in Immunology Vol 2 pp157-168 North Holland Amsterdam (1974)

11 Cowan NJ Secher DS & Milstein C "Intracellular immunoglobulin chain synthesis in non-secreting variants of a mouse myeloma: Detection of inactive light chain messenger RNA" J Mol Biol 90 691-701 (1974)

12 Ramasamy R Secher DS & Adetugbo K "CH3 domain of IgG as binding site to Fc receptor on mouse lymphocytes" Nature 253 656 (1975)

13 Milstein C Adetugbo K Brownlee GG Cowan NJ Proudfoot NJ Rabbitts TH & Secher DS "Immunoglobulin genes in a mouse myeloma and in mutant clones" in "Molecular Approaches to Imuunology" (eds Smith EE & Ribbons DW) pp131-148 Academic Press New York (1975)

14 Secher DS Gesteland RF & Milstein C "Messenger ribonucleic acids from mutant myeloma cells" Biochem Soc Trans 3 873-875 (1975)

15 Cowan NJ Secher DS & Milstein C "Purification and sequence analysis of the mRNA coding for an immunoglobulin heavy chain" Eur J Biochem 61 355-368 (1976)

16 Secher DS Adetugbo K Cowan NJ Köhler G Milstein C & Wilde CD "Variations on a theme" in "Structure-function Relationships of Proteins" (eds Markham R & Horne RW) pp129-144 North-Holland Amsterdam (1976)

17 Adetugbo K Milstein C & Secher DS "Molecular analysis of spontaneous somatic mutants" Nature 265 299-304 (1977)

18 Milstein C Adetugbo K Cowan NJ Köhler G Secher DS & Wilde CD "Somatic cell genetics of antibody-secreting cells: Studies of clonal diversification and analysis by cell fusion" Cold Spring Harbor Symp Quant Biol 41 793-803 (1977)

19 Secher DS Milstein C & Adetugbo K "Somatic mutants and antibody diversity" Immunol Rev 36 51-72 (1977)

20 Springer T Galfrè G Secher DS & Milstein C "Monoclonal xenogeneic antibodies to mouse leucocyte antigens: Identification of macrophage-specific and other differentiation antigens" Curr Topics Microbiol Immunol 81 45-53 (1978)

21 Stern P Willison K Lennox ES Galfrè G Milstein C Secher DS & Ziegler A "Monoclonal antibodies as probes for differentiation and tumour associated antigens: A Forssman specificity on teratocarcinomas and early mouse embryos" Cell 14 775-783 (1978)

22 Springer T Galfè G Secher DS & Milstein C "Monoclonal xenogeneic antibodies to murine cell surface antigens: Identification of novel leucocyte differentiation antigens" Eur J Immunol 8 539-551 (1978)

23 Milstein C Adetugbo K Cowan NJ Köhler G & Secher DS "The expression of antibody genes in tissue culture: Structural mutants and hybrid cells" Nat Cancer Inst Monogr 48 321-330 (1978)

24 Secher DS "Structure of immunoglobulins" in "Defense and Recognition" 2nd edition (ed Lennox ES) pp1-48 University Park Press Baltimore (1979)

25 Secher DS Cotton RGH Cowan NJ Gesteland RF & Milstein C "Structural mutants of immunoglobulin heavy chains" in "Nonsense Mutations and tRNA Suppressors" (eds Celis JE & Smith JD) pp285-299 Academic Press London (1979)

26 Springer T Galfrè G Secher DS & Milstein C "Mac-1: A macrophage differentiation antigen identified by monoclonal antibody" Eur J Immunol 9 301-306 (1979)

27 Milstein C Galfè Secher DS & Springer T "Monoclonal antibodies and cell surface antigens" Cell Biol Int Reports 3 1-16 (1979)

28 Milstein C Galfè Secher DS & Springer T "Monoclonal antibodies and cell surface antigens" in "Genetics and Human Biology: Possibilities and Realities" CIBA Foundation Symp 66 pp251-276 Excerpta Medica (1979)

29 Secher DS & Burke DC "A monoclonal antibody for large-scale purification of human leucocyte interferon" Nature 285 446-450 (1980)

30 Secher DS "Monoclonal antibodies by cell fusion" Immunology Today 1 22-26 (1980)

31 Janossy G Tidman N Crawford D Papageorgiou ES Prentice HG Francis G Bradstock KF McConnell I Secher DS & Milstein C "Standardisation of monoclonal antibodies for clinical studies in leukaemia / lymphoma" in "Protides of the Biological Fluids 28" (ed Peeters H) pp523-528 Pergamon Press London (1980)

32 Secher DS "Immunoradiometric assay of human leukocyte interferon using monoclonal antibody" Nature 290 501-503 (1981)

33 Morser J Meager A Burke DC & Secher DS "Production and screening of cell hybrids producing a monoclonal antibody to human interferon-α" J Gen Virol 53 257-265 (1981)

34 Scott GM Secher DS Flowers D Bate J Cantell K & Tyrrell DAJ "Toxicity of interferon" British Med J 282 1345-1348 (1981)

35 Crawford DH Francis GE Wing MA Edwards J Janossy G Hoffbrand AV Prentice HG Secher DS McConnell I Kung PC & Goldstein G "Reactivity of monoclonal antibodies with human myeloid precursor cells" Br J Haematol 49 209-217 (1981)

36 Takei F Secher DS Milstein C & Springer T "Use of a monoclonal antibody specifically non-reactive with T cells to delineate lymphocyte subpopulations" Immunology 42 371-378 (1981)

37 Scott GM Wallace J Tyrrell DAJ Cantell K Secher DS & Stewart WE "Interim report on studies on "toxic" effects of human luekocyte-derived interferon-alpha (HuIFN-α)" J Interferon Res 2 127-130 (1982)

38 Scott GM Phillpotts RJ Wallace J Secher DS Cantell K & Tyrrell DAJ "Purified interferon as protection against rhinovirus infection" Br Med J 284 1822-1825 (1982)

39 Walker JR Nagington J Scott GM & Secher DS "An immunoradiometric assay of serum interferon using a monoclonal antibody" J Gen Virol 62 181-185 (1982)

40 Hawkins RE & Secher DS "Immunoradiometric assay for interferon - characterisation of assay inhibition" in "Immunoassays for Clinical Chemistry" (eds Hunter WM & Corrie JET) pp582-587 Churchill Livingstone Edinburgh (1982)

41 Berg K Secher DS & Heron I "Purification and characterisation of the HuIFN-α species" in "Texas Reports on Biology and Medicine" (eds Baron S Dianzani F & Stanton GJ) Vol 41 pp225-233 University of Texas Galveston (1982)

42 Burke DC & Secher DS "Monoclonal antibodies to interferons" in "Interferons and their Applications" (eds Cane P & Carter C) Springer New York (1983)

43 Secher DS "Purification and assay of interferon" Biotest Bull 4 379-383 (1983)

44 Saksela E Virtanen I Hovi T Secher DS & Cantell K "Monocyte is the main producer of human leukocyte alpha interferons following Sendai Virus induction" Prog Med Virol 30 78-86 (1984)

45 King RM Burke DC Northrop F & Secher DS "Characterisation and properties of a modified human interferon-α containing an additional 18 amino acids at the N-terminus" J Gen Virol 64 1815-1818 (1983)

46 Hawkins RE Spragg JS & Secher DS "Immunopurification of HuIFN-α using two monoclonal antibodies, NK2 and YOK 5/19" Antiviral Res 1 9 (1983)

47 Stassin V Coulie PG Birshtein BK Secher DS & Van Snick J "Determinants recognised by murine rheumatoid factors: Molecular localisation using a panel of mouse myeloma variant immunoglobulins" J Exp Med 158 1763-1768 (1983)

48 Evans T & Secher DS "Kinetics of internalisation and degradation of surface-bound interferon in human lymphoblastoid cells" EMBO J 3 2975-2978 (1984)

49 Scott GM Robinson JA Secher DS Ashburner CM & Abbott SR "Measurement of interferon from *in vitro* stimulated lymphocytes by bioassay and monoclonal antibody-based immunoassay" J Gen Virol 66 1621-1625 (1985)

50 Scott GM Onwubalili JK Robinson JA Doré C Secher DS & Cantell K "Tolerance of one-month intranasal interferon" J Med Virol 17 99-106 (1985)

51 Diaz-Espada F Milstein C & Secher DS "Effect of purified human interferon-α on the expression of differentiation antigens and mitogen reactivity of cultured human thymic cells" Cellular Immunology 100 331–339 (1986)

52 Dadmarz R Evans T Secher DS Marshall N & Cawley J "The mechanism of action of interferon-α (IFN-α) in hairy cell leukaemia; Hu-IFN-α2 receptor expression by hairy cells and other normal and leukaemic cell types" Leukaemia Res 10 1279-1285 (1986)

53 Aguado MT Balderas RS Rubin RL Duchosal MA Kofler R Birshtein BK Secher DS Dixon FJ & Theofilopoulos AN "Specificity and molecular characteristics of monoclonal IgM rheumatoid factors from arthritic and non-arthritic mice" J Immunol 139 1080-1087 (1987)

54 Dorin JR Novak M Hill RE Brock DJ Secher DS & Van Heyningen V "Aclue to the basic defect in cystic fibrosis.from cloning the CF antigen.gene"..Nature 326..614-617..(1987)

55 McManus MT McKeating JA Secher DS Osborne DJ Ashford D Dwek RA & Rademacher TW "Identification of a monoclonal antibody to abscission tissue that recognises xylose/fucose-containing N-linked oligosaccharides from higher plants" Planta 175 506-512 (1988)

56 Begent RJH Ledermann JA Bagshawe KD Green AJ Kelly AMB Lane D Glaser MG Dewji MR Baker TS & Secher DS "Chimeric B72.3 antibody for repeated radio-immunotherapy of colorectal carcinoma" Antibody Immunoconjugates and Radiopharmaceuticals 3 86 (1990)

57 Einhorn N Ling P Secher DS & Strander H "Treatment of advanced condilomata acuminata with semi-purified human leukocyte interferon" Acta Oncologica (in press 1990)

58 Galfrè GL & Secher DS "Monoclonal antibodies" in "Ullmann's Encyclopaedia of Industrial Chemistry" VCH Weinheim (in press 1990)

59 Bright S Adair J & Secher DS "From clone to clinic" Immunology Today (in press 1991)